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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
ARTHUR, L	
ART UNIT	**PAPER NUMBER**
1654	15

DATE MAILED: 03/09/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)

1- File Copy

Office Action Summary

Application No.	Applicant(s)
08/962,094	Billing-Medel et al.
Examiner	**Group Art Unit**
Lisa Athur	1655

☒ Responsive to communication(s) filed on *Dec 13, 1999*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-13, 15-29, and 31-48* is/are pending in the applicat

Of the above, claim(s) *17-29, 31, 32, 34, 36, and 37* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-13, 15, 16, 33, 35, and 38-48* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. This action is in response to the paper filed December 13, 1999. Claims 14 and 30 have been canceled. Claims 1-8,10,11,15,33,38 and 39 have been amended. Claims 40-48 have been newly added. Claims 1-13, 15-29 and 31-48 are pending, but claims 17-29,31,32,34,36 and 37 have been withdrawn from consideration by the restriction requirement. Therefore, this action contains an examination of claims 1-13, 15,16,33,35,38-48. Any rejections made in the previous action which have been reiterated have been obviated by the amendments made to the claims. This action contains new grounds of rejection which have been necessitated by the amendments made to the claims. This action is FINAL. The current status of the pending claims is as follows:

I. Claims 11-16,33,38,39 and newly added claims 43-48 are rejected under 35 U.S.C. 102(b).

II. Claims 1-10,35 and newly added claims 40-42 are rejected under 35 U.S.C. 112, first paragraph

MAINTAINED REJECTIONS

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 11-16,33,38,39 and newly added claims 43-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al.(genbank accession no AA340069, from Nature 377(6547 Suppl.) 3-174 (1995)) and by Hillier et al. (Accession no. R75793, 1995)

Adams et al. Teach a 229 base pair expressed tag sequence (EST), i.e. a polynucleotide, which is about 90% identical to SEQ ID NO 1-5 of this application. (See attachment 1)

Hillier et al. Teach a 403 nucleotide EST containing clone which has 87.9%-95% sequence similarity with SEQ ID NO 1-5 of this application isolated from a human breast cDNA library (cells transfected with a vector containing the EST). (see attachment 1).

4. The response traverses the rejection on the following grounds. The response asserts that the date of entry of the Adams et al. Sequence was 21 April 1997 making this reference a reference under 35 U.S.C. 102(a) rather than 102(b). The response also argues that the present application claimed priority to application 08/742,067, filed 31 October 1996 which taught a sequence which was the same as nucleotides 14-428 of SEQ ID NO 4 while the Adams et al. Reference span nucleotides 18-311 of SEQ ID NO 4. The response concludes therefore that Adams et al. is not prior art against this application.

These arguments have been thoroughly reviewed but are deemed non-persuasive for the following reasons. First, the sequence Adams et al. Has a publication date of 1995 because this 294 nucleotide sequence of Adams et al. was published in Nature volume 377 (6547 suppl.) pp 3-174. Consequently, Adams et al. Is prior art under 35 U.S.C 102(b). Second, when assigning effective filing dates to claims, each claim is considered as a whole. Consequently, since claims

11-16., 33, 38 and 39 recite SEQ ID NO 4 which was specifically not disclosed in parent application 08/742,067, this claim as a whole is given an effective filing date of October 31, 1997. After the determination of the filing date for each claim, the art is applied. Therefore, even though the parent application disclosed as much of SEQ ID NO 4 as Adams et al., this fact is irrelevant with regard to the effective filing date of the claim unless the claims was limited to only the sequences which were disclosed in the parent application.

The response further argues none of the cited sequences teach the polypeptide sequence of SEQ ID NO 16. This argument is not convincing because none of the claims are drawn to a polypeptide. Claims 15, 38 and 46-48 are drawn to polynucleotides which encode a polypeptide containing fragments of the amino acid sequence of SEQ ID NO 16. However, because the nucleic acids of Adams and Hillier et al. are the same as the claimed nucleic acids for the reasons given above, the nucleic acids encode the same polypeptide fragments. Furthermore, none of the claimed polynucleotides encode the complete amino acids sequence given in SEQ ID NO 16.

The response also argues that Hillier et al. Only teach the full length sequence and does not teach fragments. This argument has been reviewed but is deemed non-persuasive because the claims are not limited to SEQ ID NO 1-5 or to fragments of SEQ ID nos 1-5. Instead claims 11-13 ,33, 43-45 are drawn to polynucleotides comprising a polynucleotide having at least 10, 12, 15 or 20 nucleotides that specifically bind and at least 90% identity with SEQ ID NO 1, 3. Consequently, these claims are drawn to polynucleotides that contain only 10 nucleotides that specifically bind and are 90% similar to SEQ ID NO 1 or 3 which 10 nucleotides are embedded in

a sequence which is completely different and does not meet these limitations and wherein the polynucleotide as a whole has no size limitations. Similarly, claims 15 and 16, 46-48 are drawn to an expression system and host cell, respectively, containing a polynucleotide that encodes a polypeptide of at least 8 amino acids from SEQ ID NO 16. Again these claims encompass vectors and cells containing a polynucleotide which may encode only 8 amino acids from SEQ ID NO 16 embedded within a larger sequence which has no similarity to the rest of SEQ ID NO 16. However, since Adams and Hillier et al. Teach polynucleotides with sequence identity to SEQ ID NO 1-5 and since SEQ ID No 16 is the translation product of SEQ ID NO 4,5, then Adams et al. And Hillier et necessarily teach a polynucleotide which encodes at least 8 amino acids of SEQ ID NO 16. Claims 38 and 39 are drawn to genes that encode a protein comprising 90% identity with SEQ ID NO 16 (claim 38) or comprising DNA of at least 90% identity with SEQ ID NO 4 or 5. The polynucleotides of Adams et al. And Hillier et al. Anticipate these claims because they teach polynucleotides that contain a portion which at least 90% identical to SEQ ID NO 4 or 5 or encode a portion of SEQ ID NO 16 as discussed above. As written, the claims encompass polynucleotides which have a sequence of any length, i.e. a few nucleotides that has 90% sequence similarity with the encoded sequence of SEQ ID NO 16 or the DNA sequences of SEQ ID Nos 4 and 5 because the claims to not specify that the 90% identity is over the whole length of the gene with the whole length of the recited SEQ ID NO sequence.

The response argues that the art provided no reason as to why one sequence out of the huge number of polynucleotide and polypeptide sequences would be selected to make probes or primers. This argument is not relevant because the claims are not limited to probes and primers.

Therefore, for all of the reasons given above this rejection is maintained.

NEW GROUNDS OF REJECTION

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-10,35 and newly added claims 40-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims have been amended to recite that the method is for detecting the presence of a polynucleotide indicative of breast disease by probing with a polynucleotide which has at least 10 nucleotides that specifically bind and have 90% identity with SEQ ID NO 5 and detecting the presence of the target polynucleotide indicative of breast disease. The specification teaches that SEQ ID Nos 1-3 are overlapping EST clones that were identified as being primarily representative of breast tissue libraries. SEQ ID NO 1-3 were used to make a contig which is SEQ ID NO 4 and SEQ. ID NO 5 represents the consensus sequence. SEQ ID NO 16 is the first forward frame

translation of SEQ ID NO 5 which provides a 90 amino acids sequence. SEQ ID NO 4 was compared to the EST database and was found in 85.7 % of breast libraries and only 0.2% of non-breast libraries. The specification teaches that total RNA was obtained from solid breast tissue and from non-breast tissue and used for Northern blot analysis and RT-PCR . Figures 3A and 3B show the results of a Northern blot analysis using SEQ ID NO 1 as a probe with RNA from normal breast tissue, normal prostate and cancer prostrate (3A) and from normal breast tissue and breast cancer tissue (3B). The probe hybridized with all normal breast 1/3 prostate cancer, 0 normal prostate, and 2/6 breast cancer. Table 1 showed than in 2/6 test breast cancer tissues there was over expression of the polynucleotide to which SEQ ID NO 1 hybridized. These data, however, do not support an association of expression of an mRNA to which SEQ ID NO 1 hybridizes with "breast disease". First, "diseases of the breast" is a broad term which is not limited to breast cancer but would encompass any type of disease of breast tissue, i.e. infections of breast tissue, mammary gland disorders, for example. The only breast disease tissue analyzed in the specification was breast cancer tissue. Second, the evidence in the specification does not predictably teach an association of a polynucleotide to which SEQ ID NO 1 hybridizes with breast cancer because the data is conflictory. In the northern blot analysis only two out of six breast cancer tissue samples showed expression of the polynucleotide complementary to SEQ ID NO 1. Four of the six breast cancer samples did not show expression of the polynucleotide as compared to five out of six normal breast tissue which did express the polynucleotide. From this assay, the skilled artisan would be lead to predict that the absence or decrease in expression of mRNA

complementary to SEQ ID NO 1 might by associated with breast cancer as compared to normal breast tissue. However, the data in Table 1 seems to suggest that increased expression of an mRNA complementary to SEQ ID NO 1 was associated with breast cancer. Consequently, since the teachings in the specification are limited and do not allow the skilled artisan to drawn a reasonable and predictable conclusion as to an association with breast cancer, undue experimentation would be required of the skilled artisan to practice the claimed invention. Furthermore, the specification has not provided any guidance with regard to the presence of absence of a genomic DNA sequence which hybridizes with SEQ ID NO 1-5 and breast disease. The sequence appears to be present and expressed and normal breast tissue, but no conclusions can be made as to it's presence in the genome of other tissues because no teachings have been provided in the specification.

7. No claims are allowable over the prior art.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

a shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa Arthur whose telephone number is (703) 308-3988. The examiner can normally be reached on Monday-Thursday from 7:00 AM to 1:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Lisa B. Arthur

LISA B. ARTHUR
PRIMARY EXAMINER
GROUP 1800 1600

March 8, 2000